



Clinical trial results:

A Phase IV, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Persistency of Response with or without Xolair after Long-Term Therapy (XPORT)

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2016-001001-16 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 14 August 2013 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 07 January 2017 |
| First version publication date | 07 January 2017 |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | Q4777n |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01125748 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | F. Hoffmann-La Roche AG |
| Sponsor organisation address | Grenzacherstrasse 124, Basel, Switzerland, CH-4070 |
| Public contact | F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com |
| Scientific contact | F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com |

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|----------------|
| Analysis stage | Final |
| Date of interim/final analysis | 14 August 2013 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 14 August 2013 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

This was a randomised, double-blind, placebo-controlled, 2-arm, 1-year study of subjects who completed the EXCELS study (NCT00252135) and had received long-term treatment with Xolair. In addition, subjects who did not participate in the EXCELS study but received long-term (~5 years) treatment with Xolair were allowed to enter the study.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy:

Subjects could receive 1 or more of the following medications as concomitant asthma therapy: Inhaled corticosteroids; long acting beta-agonists; zafirlukast or other leukotriene receptor antagonist; zileuton or other 5-lipoxygenase enzyme inhibitors; oral, inhaled, and/or nasal anticholinergic therapy; mast-cell stabilizers; theophyllines; chronic oral corticosteroids, defined as a minimum dose of oral prednisone of 2 to 40 mg/day or 5 to 80 mg every other day.

Evidence for comparator: -

| | |
|---|-------------|
| Actual start date of recruitment | 12 May 2010 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | United States: 176 |
| Worldwide total number of subjects | 176 |
| EEA total number of subjects | 0 |

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) | 1 |
| Adults (18-64 years) | 151 |

| | |
|---------------------|----|
| From 65 to 84 years | 24 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Subjects, who previously completed the EXCELS study and received long-term treatment with omalizumab (Xolair). In addition, subjects, who did not participate in the EXCELS study but received long-term (~5 years) treatment with omalizumab. Continuous omalizumab exposure was required prior to enrollment in this study.

Pre-assignment

Screening details:

Eligible subjects were randomised in a 1:1 ratio to continue to receive omalizumab (Xolair) at the same dose and dosing interval as administered prior to enrollment to this study (continuation group) or to receive placebo at the same dosing interval as omalizumab (Xolair) was administered prior to enrollment to this study (discontinuation group).

Period 1

| | |
|------------------------------|---------------------------------|
| Period 1 title | Overall Period (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Blinding implementation details:

The treatment designation for subjects reaching the primary efficacy endpoint (one protocol-defined severe asthma exacerbation) was unblinded to allow appropriate clinical intervention. Subjects who had their treatment designation unblinded remained in the study for ongoing evaluation of safety and were allowed to continue on study drug known to be omalizumab (or to start study drug known to be omalizumab if they were in the placebo group).

Arms

| | |
|------------------------------|------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Omalizumab |

Arm description:

Subjects received omalizumab subcutaneously at the same dose and dosing interval as administered prior to enrollment in this study. The dose of omalizumab was either a minimum of 0.008 milligrams/kilogram/Immunoglobulin E (mg/kg/IgE) (International Units/millilitre [IU/mL]) every 2 weeks or a minimum of 0.016 mg/kg/IgE (IU/mL) every 4 weeks for 48 weeks.

| | |
|--|-----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | omalizumab |
| Investigational medicinal product code | |
| Other name | Xolair |
| Pharmaceutical forms | Powder for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Omalizumab was administered subcutaneously at the same dose and dosing interval as administered prior to enrollment. The dose of omalizumab was either a minimum of 0.008 mg/kg/IgE (IU/mL) every 2 weeks or a minimum of 0.016 mg/kg/IgE (IU/mL) every 4 weeks for 48 weeks.

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description:

Subjects received matching placebo subcutaneously at the same dosing interval as omalizumab was administered prior to enrollment in this study.

| | |
|----------|---------|
| Arm type | Placebo |
|----------|---------|

| | |
|--|-----------------------------------|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Placebo contained the same ingredients as the omalizumab formulation, excluding omalizumab, and was administered subcutaneously at the same dosing interval as omalizumab was administered prior to enrollment in this study, which was every 2 weeks or every 4 weeks for 48 weeks.

| Number of subjects in period 1 | Omalizumab | Placebo |
|---------------------------------------|------------|---------|
| Started | 88 | 88 |
| Completed | 78 | 74 |
| Not completed | 10 | 14 |
| Consent withdrawn by subject | 2 | 4 |
| Physician decision | 8 | 7 |
| Adverse event, non-fatal | - | 2 |
| Lost to follow-up | - | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|------------|
| Reporting group title | Omalizumab |
|-----------------------|------------|

Reporting group description:

Subjects received omalizumab subcutaneously at the same dose and dosing interval as administered prior to enrollment in this study. The dose of omalizumab was either a minimum of 0.008 milligrams/kilogram/Immunoglobulin E (mg/kg/IgE) (International Units/millilitre [IU/mL]) every 2 weeks or a minimum of 0.016 mg/kg/IgE (IU/mL) every 4 weeks for 48 weeks.

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Subjects received matching placebo subcutaneously at the same dosing interval as omalizumab was administered prior to enrollment in this study.

| Reporting group values | Omalizumab | Placebo | Total |
|---|------------|---------|-------|
| Number of subjects | 88 | 88 | 176 |
| Age categorical Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 1 | 0 | 1 |
| Adults (18-64 years) | 78 | 73 | 151 |
| From 65-84 years | 9 | 15 | 24 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous Units: years | | | |
| arithmetic mean | 51.14 | 51.86 | |
| standard deviation | ± 11.73 | ± 13.25 | - |
| Gender categorical Units: Subjects | | | |
| Female | 63 | 60 | 123 |
| Male | 25 | 28 | 53 |

End points

End points reporting groups

| | |
|--|------------|
| Reporting group title | Omalizumab |
| Reporting group description: Subjects received omalizumab subcutaneously at the same dose and dosing interval as administered prior to enrollment in this study. The dose of omalizumab was either a minimum of 0.008 milligrams/kilogram/Immunoglobulin E (mg/kg/IgE) (International Units/millilitre [IU/mL]) every 2 weeks or a minimum of 0.016 mg/kg/IgE (IU/mL) every 4 weeks for 48 weeks. | |
| Reporting group title | Placebo |
| Reporting group description: Subjects received matching placebo subcutaneously at the same dosing interval as omalizumab was administered prior to enrollment in this study. | |

Primary: Percentage of Subjects Not Experiencing a Protocol-Defined Severe Exacerbation During the Study

| | |
|--|---|
| End point title | Percentage of Subjects Not Experiencing a Protocol-Defined Severe Exacerbation During the Study |
| End point description: A protocol-defined severe exacerbation was a clinically significant worsening of asthma which, in the clinical judgment of the investigator, required at least 1 of the following: (1) Initiation of systemic corticosteroid treatment (tablets, suspension, or injection) or an increase in the level of systemic corticosteroid treatment from a stable maintenance dose for at least 3 days (For patients taking chronic oral corticosteroids, a protocol-defined severe exacerbation was any clinically significant worsening of asthma requiring ≥ 3 days of treatment with at least a 20 mg increase in the average daily dose of oral prednisone or a comparable dose of systemic corticosteroids) or (2) a hospitalization or emergency room visit because of asthma requiring systemic corticosteroids. The Intent-to-treat (ITT) population included all randomised subjects based on randomised treatment groups regardless of actual treatment. | |
| End point type | Primary |
| End point timeframe: Baseline to end of study (up to 52 weeks) | |

| End point values | Omalizumab | Placebo | | |
|----------------------------------|-------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 88 | 88 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 67 (57.2 to 76.9) | 47.7 (37.3 to 58.2) | | |

Statistical analyses

| | |
|----------------------------|------------------------------|
| Statistical analysis title | Mean Difference between Arms |
| Comparison groups | Omalizumab v Placebo |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 176 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 19.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 5 |
| upper limit | 33.6 |

Secondary: Time to the First Protocol-defined Severe Exacerbation

| | |
|--|--|
| End point title | Time to the First Protocol-defined Severe Exacerbation |
| End point description: | |
| <p>A protocol-defined severe exacerbation was a clinically significant worsening of asthma which, in the clinical judgment of the investigator, required at least 1 of the following: (1) Initiation of systemic corticosteroid treatment (tablets, suspension, or injection) or an increase in the level of systemic corticosteroid treatment from a stable maintenance dose for at least 3 days (for subjects taking chronic oral corticosteroids, a protocol-defined severe exacerbation was any clinically significant worsening of asthma requiring ≥ 3 days of treatment with at least a 20 mg increase in the average daily dose of oral prednisone or a comparable dose of systemic corticosteroids) or (2) a hospitalization or emergency room visit because of asthma requiring systemic corticosteroids. The ITT population included all randomised subjects based on randomised treatment groups regardless of actual treatment.</p> | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline to end of study (up to 52 weeks) | |

| End point values | Omalizumab | Placebo | | |
|---|-----------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 88 | 88 | | |
| Units: Weeks | | | | |
| arithmetic mean (confidence interval 95%) | 21.7 (14.41 to 29.03) | 16.6 (11.9 to 21.26) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline to end of study (up to 52 weeks)

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 16.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|------------|
| Reporting group title | Omalizumab |
|-----------------------|------------|

Reporting group description:

Subjects received omalizumab subcutaneously at the same dose and dosing interval as administered prior to enrollment in this study. The dose of omalizumab was either a minimum of 0.008 mg/kg/IgE (IU/mL) every 2 weeks or a minimum of 0.016 mg/kg/IgE (IU/mL) every 4 weeks for 48 weeks. The safety population for omalizumab exposure included all subjects who received at least one injection of omalizumab while on study. In addition, subjects from the placebo arm who 'crossed over' and were given omalizumab after an unblinding exacerbation were included.

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Subjects received matching placebo subcutaneously at the same dosing interval as omalizumab was administered prior to enrollment in this study. The safety population included all subjects who received at least one injection of placebo while on study.

| Serious adverse events | Omalizumab | Placebo | |
|---|------------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 10 / 121 (8.26%) | 8 / 88 (9.09%) | |
| number of deaths (all causes) | 0 | 1 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Adenocarcinoma of colon | | | |
| subjects affected / exposed | 1 / 121 (0.83%) | 0 / 88 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mueller's mixed tumour | | | |
| subjects affected / exposed | 0 / 121 (0.00%) | 1 / 88 (1.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Injury, poisoning and procedural complications | | | |
| Laceration | | | |

| | | | |
|--|-----------------|----------------|--|
| subjects affected / exposed | 1 / 121 (0.83%) | 0 / 88 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Haematoma | | | |
| subjects affected / exposed | 1 / 121 (0.83%) | 0 / 88 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Syncope | | | |
| subjects affected / exposed | 1 / 121 (0.83%) | 0 / 88 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Spontaneous haematoma | | | |
| subjects affected / exposed | 1 / 121 (0.83%) | 0 / 88 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Dyskinesia oesophageal | | | |
| subjects affected / exposed | 1 / 121 (0.83%) | 0 / 88 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dysphagia | | | |
| subjects affected / exposed | 1 / 121 (0.83%) | 0 / 88 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eosinophilic oesophagitis | | | |
| subjects affected / exposed | 1 / 121 (0.83%) | 0 / 88 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |

| | | | |
|--|-----------------|----------------|--|
| subjects affected / exposed | 6 / 121 (4.96%) | 4 / 88 (4.55%) | |
| occurrences causally related to treatment / all | 2 / 6 | 2 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 121 (0.00%) | 1 / 88 (1.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 121 (0.00%) | 1 / 88 (1.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Intervertebral disc degeneration | | | |
| subjects affected / exposed | 1 / 121 (0.83%) | 0 / 88 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 121 (0.00%) | 1 / 88 (1.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 121 (0.00%) | 1 / 88 (1.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Omalizumab | Placebo | |
|---|-------------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 98 / 121 (80.99%) | 71 / 88 (80.68%) | |
| Nervous system disorders | | | |

| | | | |
|---|-------------------------|------------------------|--|
| Headache subjects affected / exposed occurrences (all) | 5 / 121 (4.13%) 7 | 3 / 88 (3.41%) 3 | |
| Respiratory, thoracic and mediastinal disorders Asthma subjects affected / exposed occurrences (all) | 36 / 121 (29.75%) 62 | 33 / 88 (37.50%) 38 | |
| Rhinitis allergic subjects affected / exposed occurrences (all) | 1 / 121 (0.83%) 1 | 7 / 88 (7.95%) 8 | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 6 / 121 (4.96%) 7 | 2 / 88 (2.27%) 2 | |
| Infections and infestations Acute sinusitis subjects affected / exposed occurrences (all) | 13 / 121 (10.74%) 15 | 11 / 88 (12.50%) 15 | |
| Bronchitis subjects affected / exposed occurrences (all) | 9 / 121 (7.44%) 10 | 8 / 88 (9.09%) 9 | |
| Sinusitis subjects affected / exposed occurrences (all) | 27 / 121 (22.31%) 36 | 13 / 88 (14.77%) 18 | |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 24 / 121 (19.83%) 28 | 11 / 88 (12.50%) 12 | |
| Urinary tract infection subjects affected / exposed occurrences (all) | 6 / 121 (4.96%) 13 | 6 / 88 (6.82%) 7 | |
| Viral upper respiratory tract infection subjects affected / exposed occurrences (all) | 6 / 121 (4.96%) 6 | 3 / 88 (3.41%) 3 | |
| Gastroenteritis viral subjects affected / exposed occurrences (all) | 6 / 121 (4.96%) 7 | 1 / 88 (1.14%) 1 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|---|
| 15 October 2010 | Protocol Q4777n was amended to increase the percent allowance of missed doses from the beginning of EXCELS to enrollment to XPORT (from 10% to 25%); and from maximum of 1 to maximum of 2 doses within the last 6 months before being randomised into XPORT. The original inclusion criteria which required "no more than 3 months between completion of EXCELS and the screening visit for XPORT" has been removed. Subjects should have continued to receive Xolair therapy between completion of EXCELS and enrollment to XPORT to be eligible for this study. In addition, Serious Adverse Events (SAE) reporting period has been updated to 24 hours for all SAE types. |
| 12 July 2011 | Protocol Q4777n was amended to allow subjects to enter the study who did not participate in EXCELS but received long-term (~5 years) treatment with Xolair. Additional minor changes have been made to improve clarity and consistency. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported